CLAIMS

1. A method of identifying subjects having a high or low drug metabolising phenotype associated with cytochrome CYP3A5 expression, which method comprises the steps of:

screening genomic DNA from said subject for the presence or absence of one or more polymorphic variants in a transcription regulatory region of the sequence encoding CYP3A5 characteristic of a high drug metabolising phenotype.

2. A method of screening human subjects for suitability for treatment with a drug metabolised by CYP3A5 comprising screening for the presence or absence of one or more polymorphic variants in a transcription regulatory region of the sequence encoding CYP3A5 characteristic of a high drug metabolising phenotype.

3. A method according to claim 1 or 2 comprising screening for said one or more variants in a recognition site for a transcription factor of said regulatory region.

4. A method according to any of claims 1 to 3 comprising screening for said one or more variants in an activator protein-3 motif (AP-3) and/or basic transcription element (BTE).

5. A method according to any of claims 1 to 4, comprising screening for said one or more variants at any one of positions -475 or -147 of the transcription regulatory region of the sequence encoding CYP3A5 the sequence of which region is illustrated in Figure 7.

6. A method according to claim 5 comprising screening for both of said variants at position -475 or -147 of said transcriptional regulatory region of CYP3A5.

7. A method according to any of claims 1 to 5 wherein said DNA is amplified using oligonucleotide molecules which are capable of hybridising selectively to the wild type or variant sequences respectively such that generation of amplified DNA from said respective molecules will indicate whether said wild type or said variant is present.

8. A method of identifying one or more polymorphic variants in a transcription regulatory region of DNA encoding cytochrome CYP3A5 said method comprising the steps of:

1) subjecting the sample DNA to amplification using oligonucleotide molecules which are capable of selectively hybridising to the wild type and/or said one or more variant sequences, which molecules are such that they can introduce a restriction site in one of said amplified wild type or variant sequences, and

2) subjecting amplified DNA from step 1 to restriction with an enzyme which cleaves at said restriction site to provide a restriction digest indicative of the presence or absence of said mutation.

9. A method according to claim 8 wherein said molecule introduces a restriction site in a region corresponding to a recognition site for a transcription factor of said regulatory region.

10. A method according to claim 8 or 9 wherein said molecule introduces a restriction site in a region corresponding to an activator protein-3 motif (AP-3) and/or a basic transcription element (BTE).

11. A method according to claim 10 wherein said molecule is capable of introducing a restriction site only when the wild type A nucleotide is present at position -147 of the transcription regulatory region.

12. A method according to claim 11 wherein said restriction site is for the Tai I restriction enzyme.

13. A method according to claim 11 or 12 wherein said oligonucleotide molecule comprises the sequence designated 3A5R1 illustrated in Figure 6.

14. A method according to claim 10 wherein said molecule is capable of introducing a restriction site when the wild type T nucleotide is present at position -475 of the regulatory control region.

15. A method according to claim 14 wherein said restriction site is for the Alu I enzyme.

16. A method according to claim 14 or 15 wherein said molecule comprises the sequence designated 3A5F2 illustrated in Figure 6.

17. An oligonucleotide molecule of at least 10 contiguous nucleotides for use in amplification of a DNA sequence to detect a wild type or polymorphic variant in a transcription regulatory region of the sequence encoding cytochrome CYP3A5 said associated with a high or low drug metabolising phenotype

respectively, which molecule is capable of hybridising to a region incorporating either a polymorphic variant or wild type nucleotide in said region, such that amplification of said wild type and polymorphic variants will proceed from said molecule only when an oligonucleotide includes a sequence corresponding to either said wild type or polymorphic variant characteristic of a high drug metabolising phenotype.

18. A molecule according to claim 17 which is capable of hybridising to a recognition site for a transcription factor of said regulatory region.

19. A molecule according to claim 17 or 18 which is capable of hybridising to an activator protein-3 motif (AP-3) or a basic transcription element.

20. A molecule according to any of claims 17 to 19 which is capable of hybridising to a region comprising a polymorphic variant at any of positions -475 or -147 of the transcription regulatory region of the sequence encoding CYP3A5 illustrated in Figure 7.

21. A molecule according to any of claims 17 to 20 which comprises any of the sequences designated 3A5F1, 3A5F2 or 3A5R1 illustrated in Figure 6.

22. A kit for performing the method of any of claims 1 to 7 comprising an oligonucleotide molecule according to any of claims 17 to 21 and means for contacting said molecule and said transcription regulatory region of the sequence encoding CYP3A5.

23. A kit according to claim 22 further comprising a restriction enzyme capable of producing a

restriction digest for distinguishing between said variant or wild type sequences.

24. A kit according to claim 23 wherein said enzyme comprises any of *Tai* I or *Alu* I.

25. A method of identifying toxic or mutagenic effects of a test compound, such as, a drug, toxin or procarcinogen metabolised by CYP3A5 the method comprising contacting each of a cell having a high drug metabolising phenotype and a cell having a low metabolising phenotype associated with cytochrome CYP3A5 expression, with said test compound and identifying the effects of said compound on each of said high or low drug metabolising phenotype cells or other cells sensitive to said compound.

26. A method of diagnosing susceptibility of an individual to a disease associated with environmental toxins or procarcinogens metabolised by CYP3A5, which method comprises screening for the presence or absence of a polymorphic variant in a transcription regulatory region of the sequence encoding CYP3A5.

27. A method according to claim 26 comprising screening for said variant in a recognition site for a transcription factor of said regulatory region.

28. A method according to claim 26 or 27 comprising screening for said variant in an activator protein-3 motif (AP-3) and/or a basic transcription element (BTE) of said transcription regulatory region.

29. A method according to any of claims 26 to 28, comprising screening for said variant at any one

of position -475 or -147 of the transcription regulatory region of the sequence encoding CYP3A5 the sequence of which region is illustrated in Figure 7.

30. A method according to any of claims 26 to 29 comprising screening for both variants at position -475 or -147.

31. A method according to any of claims 26 to 30 comprising screening for the presence or absence of variants $T_{-475}G$ and $A_{-147}G$ in said transcriptional regulatory control region.

32. A method of providing a measure of activity of a transcription regulatory region of a DNA sequence encoding cytochrome CYP3A5 or of identifying a polymorphic variant which alters transcription of cytochrome CYP3A5, the method comprising providing a DNA construct having a sequence encoding a reporter molecule operably linked to a DNA fragment comprising said transcription regulatory region, and introducing said construct into a cell and monitoring for the level of expression of said reporter molecule.

33. A method of identifying transcription factors capable of hybridising to a DNA sequence from a transcription regulatory region adjacent to DNA encoding cytochrome CYP3A5, said method comprising contacting said DNA sequence including said transcription regulatory region with potential transcription factors and identifying any transcription factor complexed to said DNA sequence.

34. A method of identifying compounds acting on a transcription regulatory region of a DNA sequence encoding CYP3A5, the method comprising transforming a cell with a DNA construct comprising the sequence of said regulatory region, and which regulatory region is operably linked to a sequence encoding a reporter molecule, contacting said cell with a test compound and identifying any altered expression of said reporter molecule.

35. A method of purifying transcription factors from a sample which are capable of binding to DNA from a transcription regulatory region of a sequence encoding cytochrome CYP3A5, the method comprising contacting a DNA sequence including said transcriptional regulatory region with a mixture of transcription factors and identifying any complexes of said transcription factors and said sequence.

36. A method according to any of claims 32 to 35 wherein said transcription regulatory region includes a mutation in a recognition site for a transcription factor of said regulatory region.

37. A method according to any of claims 32 to 36 wherein said mutation occurs in an activator protein-3 motif (AP-3) and/or a basic transcription element(BTE).

38. A method according to any of claims 36 or 37 wherein said mutation occurs at any one of positions -475 or -147 of the transcription regulatory region adjacent to the sequence encoding CYP3A5, the sequence of which region is illustrated in Figure 7.

39. A method according to any of claims 32 to 38 wherein the transcription regulatory region comprises the mutations $T_{-475}G$ and $A_{-147}G$.